# Anti-inflammatory Activity of Some Essential Oils

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**Abstract**

There are many diseases that are associated with inflammation, such as infections by bacteria, virus and protozoa, autoimmune diseases such as arthritis and diabetes, Alzheimer's disease, and cancer. There are many medications available to prevent or minimize the progression of the inflammation; they include non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, but they have some secondary effects. Traditional medicine has been used to address the health demands of the population and nowadays it presents many opportunities in health care. Essential oils are use in this medicine to treat many diseases.

In a review of the last five years it was found that several essential oils with anti-inflammatory activity were isolated from 43 plants. In some cases, oils of the same genus but different species have this activity, such as the essential oils obtained from three species of genus *Origanum*, as well as three oils from three species of the *Citrus* genus, and three from the *Pimpinella* genus. In many cases the essential oil composition obtained has been determined, and in some cases the anti-inflammatory activity of the main compounds of these essential oils has been evaluated, such as carvacrol and isoeugenol, which showed an important anti-inflammatory activity. On the basis of this review, we can say that some essential oils could be an important source for the treatment of inflammatory diseases.

**Key Word Index**

Anti-inflammatory activity, essential oils, inflammatory diseases, review.

## Introduction

Inflammation is a physiological response to a variety of agents including infectious microorganisms, toxic chemical compounds and physical injury. There are many diseases that are associated with the inflammation process, such as skin inflammation (1, 2), autoimmune diseases such as arthritis and diabetes, Alzheimer's disease and cancer.

Many medications are available to prevent or minimize the progression of inflammation, includuing non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. NSAIDs such as acetyl salicylic acid, ibuprofen, diclofenac and their new related compounds are mainly selective COX-2 inhibitors; cyclooxygenase-2 is involved in the inflammation pathway. The regular use of NSAIDs can cause a number of side effects, some of which may be very serious. The most common are increases in the development of ulcers in the stomach and duodenum, as well as inhibition of uterine motility and hypersensitivity reaction (3), nausea, vomiting, indigestion, diarrhea, heartburn, headache, dizziness, rapid weight gain and breathing problems (4). The lengthy use of corticosteroids could produce the suppression of the function of pituitary-adrenal, hyperglycemia and increase susceptibility to infections (5).

The biological activities of many plants have been long known in ethnomedicine to treat inflammatory diseases. These biological properties are often due to essential oils contained in plants which are used as herbal remedy in traditional medicine. It has been found that these essential oils possess different activities such anti-inflammatory and antiradical properties (6-8). For this reason, we did a review of the last five years and in this period we found that several essential oils with anti-inflammatory activity were isolated from 43 plants.

## Essential oils with anti-inflammatory properties

***Afromomum danielli*** (Hook f.) Schum and ***A. melegueta*** Schum (Zingiberaceae): The analysis of the chemical composition of *A. melengueta* seed essential oil indicated that it is rich in sesquiterpenes. The other samples were rich in monoterpenes like limonene, 1,8-cineole, α- and β-pinenes, linalool and (E)-β-ocimene as the major components. The anti-inflammatory activity of *A. daniellii* seed essential oil was measured and gave an inhibition concentration 50 ($IC_{50}$) of 237 ppm against 0.7 ppm for nordihydroguiaretic acid (NDGA). The results achieved highlight the potential of essential oils to be developed against inflammatory disorders (9).

***Ageratum fastigiatum*** R. M. King et H. Rob. (Asteraceae): This plant is used in folk medicine as an anti-inflammatory, analgesic and antimicrobial**.** The main compounds found

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in the essential oil were germacrene D, α-humulene and β-cedrene. The oil, with $LD_{50}$ of 2.50 g/kg, inhibited the acetic acid-induced writhing at the dose of 200 mg/kg in the formalin test. In the hot plate test, after 30 min and 60 min of treatment, doses of 100 and 200 mg/kg increased the reaction time. The anti-edematogenic effect, reduction on the exudate volume and leukocyte mobilization were observed at doses of 100 and 200 mg/kg. *A. fastigiatum* possessed analgesic and anti-inflammatory properties (10).

***Aucoumea klaineana*** Pierre (Burseraceae): α-Pinene, α-phelandrene, *p*-cymene and 1,8-cineole were the major components of the essential oil. The anti-inflammatory activity was carried out by lipoxygenase method and the oil was not active (11).

***Canarium scheinfurthii*** Engl. (Burseaceae): This plant grows in Cameroon; the main components of the essential oil obtained by hydrodistillation were *p*-cymene, limonene and α-terpineol. The oil had anti-inflammatory activity in lipoxygenase method with an $IC_{50}$ of 62.6 ppm (11).

***Calycorectes sellowianus*** O. Berg (Myrtaceae): It is endemic to Brazil. The major constituents of 37 compounds of the leaves' essential oil (GC/MS) were guaiol (13.1%) and β-caryophyllene (8.6%). The anti-inflammatory activity of this oil was investigated *in vitro* and *in vivo*. It reduced the treated neutrophils chemotaxis with 91% inhibition and had no effect on the carrageenan-induced paw edema (12).

***Cinnamomum insularimontanum*** Hayata (Lauraceae): It has a strong fragrance and has been used as a folk medicine in Taiwan for a long time. The fruit essential oil was analyzed by GC/MS; the main constituents were α-pinene (9.45%), camphene (1.70%), β-pinene (4.30%), limonene (1.76%), citronellal (24.64%), citronellol (16.78%) and citral (35.89%). The results obtained from nitric oxide (NO) inhibitory activity assay, essential oil and its dominant compound (citral) presented the significant NO production inhibitory activity, $IC_{50}$ of essential oil and citral were 18.68 and 13.18 µg/mL, respectively. Moreover, based on the results obtained from the protein expression assay, the expression of IKK, iNOS, and nuclear NF-κB was decreased and I Bα was increased in dose dependent manners. It proved that the anti-inflammatory mechanism of citral was blocked via the NFjB pathway, but it could not efficiently suppress the activity on COX-2. In addition, citral exhibited a potent anti-inflammatory activity on croton oil-induced mice ear edema, at doses of 0.1 and 0.3 mg per ear. The inhibition was 22% and 83%, respectively. The results presented that the fruit essential oil of *C. insularimontanum* and citral have anti-inflammatory effect. (13).

***Cinnamomum osmophloeum*** Kaneh (Lauraceae): It is an endemic tree that grows in natural hardwood forest of Taiwan. The leaf essential oil components showed inhibitory effects as anti-bacterial, anti-termite, anti-mites, anti-mildew, anti-mosquito larvae, and anti-fungal. The chemical constituents of the essential oil were analyzed by GC/MS and they were found to be L-bornyl acetate (15.89%), caryophyllene oxide (12.98%), γ-eudesmol (8.03%), β-caryophyllene (6.60%), T-cadinol (5.49%), ð-cadinene (4.79%), *trans*-β-elemenone (4.25%), cadalene (4.19%), and *trans*-cinnamaldehyde (4.07%). The effects of essential oil on oxide NO and prostaglandin $E_2$ production in lipopolysaccharide (LPS)-activated RAW 264.7 macrophages were also examined. Results of nitric oxide tests indicated that the essential oil and its major constituents such as *trans*-cinnamaldehyde, caryophyllene oxide, L-borneol, L-bornyl acetate, eugenol, β-caryophyllene, *E*-nerolidol, and cinnamyl acetate have anti-inflammatory activity (14).

***Citrus aurantium*** L. var bergamia (Rutaceae): The essential oil is extracted from the peel of the fruit, whose main components are limonene (40%), linalool (8%) and linalyl acetate (28%) (15). The anti-inflammatory activity of essential oil of Bergamot (BO) was tested on carrageenan-induced rat paw edema at different doses: 0.025, 0.05 and 0.1 mL/kg; the reduction in paw edema was 27.56%, 30.77% and 63.93% respectively, and indomethacin used as a reference produced an inhibition of 95.7%. These results showed that BO possesses anti-inflammatory effect (16).

***Citrus sinensis*** L. (Rutaceae): Orange essential oil can be attributed to its properties like anti-inflammatory, antidepressant, anti-spasmodic, antiseptic, aphrodisiac, carminative, diuretic, tonic, sedative and cholagogue. The anti-inflammatory activity of the oil was tested using the lipoxygenase enzymatic method; the $IC_{50}$ was 20.3 mg/L (17).

***Citrus sunki*** (Hayata) Tanaka (Rutaceae): *C. sunki* is used in traditional medicine for digestion, cold, and fever. The analysis of the essential oil of this plant by GC/MS showed that the major components were dl-limonene (68.18%) and β-myrcene (4.36%). The oil reduced the LPS-induced secretion of NO in RAW 264.7 cells. This result suggests that the essential oil has anti-inflammatory activity (18).

***Cleistocalyx operculatus*** Roxb. (Myrtaceae): In folk medicine in China, Vietnam and some other tropical countries, it is widely used for the treatment of gastric ailments and as an antiseptic agent. The anti-inflammatory activity of the essential oil of *C. operculatus* buds inhibited lipopolysaccharide induced secretion of pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-1 β (IL-1β) in RAW 264.7 cells, a mouse macrophage-like cell line. Also the mRNA expression of TNF-α and IL-1β was suppressed. Moreover, reporter gene analysis revealed that the oil blocked LPS-induced transcriptional activation of NF-κB in RAW 264.7 cells. Besides, the essential oil inhibited the ear edema induced by TPA (19).

***Cordia verbenacea*** DC (Boraginaceae): This plant is a medicinal plant popularly used in Brazil as anti-inflammatory, antiulcer and anti-rheumatic agent without detailed pharmacological and toxicological studies (20). α-Humulene and *trans*-caryophyllene were identified in *C. verbenacea* essential oil and the anti-inflammatory activity of the both compounds was evaluated in a model of acute inflammation in rat paw, induced by LPS. The treatment with α-humulene or *trans*-caryophyllene inhibited the LPS-induced NF-κB activation and neutrophil migration; however, only α-humulene prevented the production of cytokines TNF-α and IL-1β and the *in vivo* up-regulation of kinin $B_1$ receptors, so that both sesquiterpenes might be used as agents to treat inflammatory diseases (21).

***Cyperus esculentus*** L. and ***C. rotundus*** Linn. (Cyperaceae): Anti-inflammatory, anti-arthritic, analgesic and anticonvulsant activities of the oils of both plants were study. Phytochemical tests of the oil are positive for flavonoids, triterpenoids, carbohydrates and proteins. The effects of the oils

were evaluated in the models of carrageenan-induced edema, formaldehyde induced arthritis, formalin induced writhing and MES induced convulsion. It was found that both essential oils posses good anti-inflammatory, anti-arthitic, analgesic and anticonvulsant activities (22).

***Chenopodium album*** L. (Chenopodiaceae): This plant is commonly known as pigweed and in folk medicine is used as laxative, antihelmitic, against round and hook worms, and as a blood purifier. Also it is used for the treatment of hepatic disorders, spleen enlargement, intestinal ulcers and burns (23). The analysis of the essential oil of *C. album* leaves revealed that the main constituents were *p*-cymene (40.9%), ascaridole (15.5%), pinane-2-ol (9.9%), α-pinene (7.0%), β-pinene (6.2%) and α-terpineol. The oil had strong anti-inflammatory activity against TPA-induced ear edema in mice (24).

***Dennettia tripetala*** G. Baker (Annonaceae): The fruit, bark, leaves and roots are used as spices and condiments. The leaves are used in combination with other medicinal plants to treat fever, typhoid, cough, worm infestation, vomiting and stomach upset (25). Atinociceptive and anti-inflammatory activity of the essential oil were tested in mice using the hot plate, acetic acid-induced writhings and formalin tests, while carrageenan-induced paw edema as anti-inflammatory model. The anti-inflammatory activity of the oil was comparable to dexamethasone (1 mg/kg) (26).

***Drimys brasiliensis*** Miers (Winteraceae): This species has been used in folk medicine as analgesic and anti-inflammatory. The essential oils from leaves and stem barks were characterized by GC-FID and GC/MS. The main components were monoterpenes (leaves 4.31% and stem barks 90.02%) and sesquiterpenes (leaves 52.31% and stem barks 6.35%). The evaluation of antinociceptive and anti-inflammatory potential of the essential oils and the sesquiterpene polygodial were evaluated in paw edema induced by carrageenan and formalin test in mice. The essential oil obtained from the stem barks significantly reduced the edema induced by carrageenan. The anti-inflammatory effect of stem barks oil (at 200 mg $kg^{-1}$) was similar to that observed with indomethacin (at 10 mg $kg^{-1}$) 30 and 60 min after the administration of essential oils. The effect of polygodial (at 200 mg $kg^{-1}$) was lower than the oils (27).

***Fortunella japonica*** (Thunb.) Swingle (Rutaceae): *F. japonica* is also known as round kumquat or Marumi kumquat. The fruit is rich in vitamins A and C. The main components of the essential oil are dl-limonene (61.58%) and carvone (6.36%). The oil significantly reduced LPS-induced NO release in RAW 264.7 cells. This fact indicates that this oil has anti-inflammatory effect (18).

***Hedychium coronarium*** Koen. (Zingiberaceae): It is commonly known as butterfly ginger, cinnamon jasmine, gargland flower and ginger lily. The rhizome has been used for the treatment of headache, diabetes, contusion inflammation and sharp pain due to rheumatism. Twenty-nine components were identified in the flowers essential oil and the main components were β-*trans*-ocimenone (28.05%), linalool (18.52%), 1,8-cineole (11.35%), α-terpineol (7.11%), 10-epi-γ-eudesmol (6.06%), sabinene (4.59%) and terpinen-4-ol (3.17%). At doses of 100 mg/kg p.o. the oil produced significant inhibition of carrageenan-induced hind paw edema in rats (28).

***Illicium anisatum*** Hayata (Illiciaceae): It is widely used for treatment of some skin problems in traditional Chinese medicine. The fruit is an important source of essential and volatile oil. Fifty-two components were identified in the essential oil and the main components were eucalyptol (21.8%), sabinene (5.3%), α-terpinenyl acetate (4.9%), kaurene (4.5%), isopimaradiene (3.2%), safrol (2.7%), β-linalool (2.6%), γ-cadinene (2.2%), α-cadinol (2.2%) and terpinen-4-ol (1.9%). The mechanism of the anti-inflammatory activities of *I. anisatum* essential oil (IAE) was evaluated whether it could modulate the production of nitric oxide (NO) and prostaglandin $E_2$ ($PGE_2$) by activated macrophages. The results indicate that IAE is an effective inhibitor of LPS-induced NO and $PGE_2$ production in RAW 264.7 cells. These inhibitory activities were accompanied by dose-dependent decreases in the expression of iNOS and COX-2 proteins and iNOS and COX-2 mRNA. Also was evaluated the cytotoxic effects of the oil, It was found that IAE exhibited low cytotoxicity at 100 mg $mL^{-1}$ (29).

***Lippia sidoides*** Cham. (Verbenaceae): It is mainly used as an antiseptic (30). It was found that the topical application of leaf essential oil at doses of 1 and 10 mg/ear, respectively, reduced 45.93% and 32.26% the acute ear edema induced by 12-O-tetradecanoylforbol 13-acetate (TPA).

***Melaleuca alternifolia*** Maiden et Betche (Myrtaceae): It has well established traditional and folk uses in Australia, specially as an antiseptic. The major constituent from the essential oil was terpinen-4-ol. This compound is considered, together with α-terpinene, γ-terpinene, and α-terpineol, the main responsible for the anti-inflammatory activity from this essential oil. The oil showed anti-inflammatory activity on edema-induced by histamine in mice. Several clinical studies and observations, endorse the clinical external use of the oil for the treatment of vulvovaginitis, mainly candidiasic cases (31).

***Mezoneuron benthamianum*** Baill. (Caesalpinoideae): This plant is used for the treatment of dermal infection, healing of refractory sores, blood disorders, as a laxative, for stomach troubles, eye treatments, genital stimulants/depressants, hemorrhoids, pain-killers, pulmonary troubles and as a chewing stick. The oil contained 15 compounds and the main components were 3-carene, pinene (11.8%), *trans*-nerolidol (13.5%), farnesene (11.6%) and thujene (6.7%). The essential oil was tested at different concentrations for its anti-inflammatory activity evaluated as inhibition of TPA induced ear edema in mice. The oil at 5.0 mg and 2.5 mg dose levels exhibited a significant anti-inflammatory activity with percentage edema reduction of 92.3% and 76.9%, respectively (32).

***Myrciaria tenella*** (DC.) Berg. (Myrtaceae): It is known as Cambuí. The GC/MS analysis revealed that the main constituents of the leaf essential oil were β-caryophyllene (25.1%) and spathulenol (9.7%). The oil reduced significantly the treated neutrophil chemotaxis with 93% inhibition, and in the systemic treatment at doses of 50 mg/kg p.o. reduced the carrageenan-induced paw edema with a similar effect for indomethacin (10 mg/kg), the positive control (33).

***Nepeta cataria*** L. var. *citriodora* (Becker) (Lamiaceae): It is used as anti-tussive, expectorant and antiathmatic (34). The essential oil was analyzed by gas chromatography-flame ionization detector (GC-FID), four major components were identified *trans,trans*-nepetalactone, *cis,trans*-nepetalactone, *trans,cis*-nepetalactone and nepetalactol. At doses of 0.0005

mL/kg the oil presented peripheric anti-inflammatory properties by reducing the induced edema after carrageenan injection (35).

***Ocotea quixos*** Lam. (Lauraceae): The main components of the essential oil were *trans*-cinnamaldehyde (27.9%) and methyl cinnamate (21.6%) (36). The anti-inflammatory activity of the essential oil and these two compounds were investigated in *in vitro* and *in vivo* models. The oil and *trans*-cinnamaldehyde, but not methyl cinnamate, significantly reduced LPS-induced NO release from J774 macrophages, inhibited LPS-induced COX-2 expression, and increased forskolin-induced cAMP production. At doses of 30-100 mg/kg of essential oil and 10 mg/kg of *trans*-cinnamaldehyde showed anti-inflammatory activity against paw edema in rats carrageenan-induced without damaging gastric mucosa (37).

***Olea europea*** L. (Oleaceae): In Tunisian folk medicine this plant is used in the treatment of inflammatory diseases and bacterial infections. The analysis of the essential oil resulted in the identification of 32 compounds and the major compounds were α-pinene (52.7%), 2,6-dimethyloctane (16.57%) and 2-methoxy-3-isopropylpyrazine (6.01%). Intraperitoneal administration of *O. europea* essential oil at doses of 100, 200 and 300 mg/kg reduced acetic acid-induced abdominal constrictions and paw edema (38).

***Origanum ehrenbergii*** Boiss and ***O. syriacum*** L. (Lamiaceae): In the essential oil of *O. ehrenbergii* was found 37 components of which thymol (19%) and *p*-cymene (16.1%) were the main abundant compounds. Thirty-six components were found in the *O. syriacum* essential oil and the main compounds were thymol (24%) and carvacrol (17.6%). *O. ehrenbergii* oil inhibited NO production in the murine monocytic macrophage cell line RAW 264.7 with an $IC_{50}$ value of 66.4 µg/mL (39).

***Origanum vulgare*** L. (Labiatae): It is an aromatic plant of the Mediterranean flora that has been commonly used to treat diarrhea and pain. Identified in the essential oil were *trans*-sabinene hydrate, thymol and carvacrol. THP-1 macrophages were used as cellular model of atherogenesis and the release/secretion of cytokines (TNT-a, IL-1b, IL-6 and IL-10) and their respective mRNA expressions were quantified both in presence or absence of supercritical oregano extracts. The results showed a decrease in pro-inflammatory TNF-a, IL-1b and IL-6 cytokines synthesis, as well as an increase in the production of anti-inflammatory cytokine IL-10. These results may suggest an anti-inflammatory effect of oregano extracts and their compounds in a cellular model of atherosclerosis (40).

***Pelargonium graveolens*** L'Hér (Geraniaceae): This plant is commonly known as geranium. For many years in traditional medicine it has been used as an anti-asthmatic, anti-allergic, antioxidant, anti-diarrheic, antihepatotoxic, diuretic, tonic, haemostatic, stomachic and anti-diabetic (41). The main components of the essential oil were citronellol (26%), citronellyl formate (16%), linalool (10%), geraniol (8%), isomenthone (6%) and menthone (4%). It was found that this essential oil could inhibit the LPS-elicited expression of the induced proinflammatory enzymes COX-2 and iNOS, as well as the NO produced by LPS-activated microglial cells. This inhibition did not result from a cytotoxic effect of the oil. Although high concentrations of citronellol could inhibit NO production from the cells, when administered at their natural relative concentrations in the oil, neither citronellol nor the other constituents of the oil were effective at inhibiting NO production (42).

***Pimpinella corymbosa*** Boiss**,** ***P. tragium*** Vill. and ***P. rhodanta*** Bois (Apiaceae): *Pimpinella* species have been used as animal feed to increase milk secretion (43), also the estrogenic activity of some isolated compounds and essential oils of different *Pimpinella* species were reported. The oils of these three species were effective in inhibiting NF-κB mediated transcription. The roots showed notably potent activities with $IC_{50}$ values of 2, 3 and 6 µg/mL, respectively (44).

***Rosmarinus officinalis*** L. (Labiatae): It is known as a common herb and household plant broadly used all around the world for different medicinal purposes, being a component of various established anti-inflammatory plant drug preparations, and having a long tradition of use for treating headaches, colds and colic, as well as other diseases (45). The effect of *R. officinalis* essential oil dietary administration at concentrations of 1250, 2500 and 5000 ppm in carrageenan paw edema and trinitrobenzene sulfonic acid (TNBS) colitis was studied (46). Dietary supplementation with 5000 ppm of the oil initially increased after 2 h, but after 24 h suppressed the extent of paw edema, and in the TNBS model exhibited protective effects on colonic mucosa and decreased macroscopic scores for colonic inflammation.

***Sabina virginiana*** L. Antoine (Cupressaceae): It is commonly known as eastern west cedar and has been used in the treatment of psoriasis, dermatitis, hemorrhoids and varicose veins. The leaves are found to exert effects on emmenagogue, as a stimulant, and as a diaphoretic in rheumatism (47). The leaves' essential oil was analyzed by GC/MS; 31 compounds were identified, and the major constituents were limonene (32.9%), safrole (23.0%), asarone (15.9%) and α-pinene (5.2%). The essential oil was tested at different concentrations (0.075, 1.25, 2.5 and 5.0 mg/ear) for its anti-inflammatory assay evaluated as inhibition of TPA induced ear edema in mice. At doses of 5.0 mg/ear the inhibition was 66.7%. This effect was similar to that obtained with indomethacin (57.7%) (48).

***Thymus vulgaris*** L. (Labiatae): Thyme has been used for respiratory ailments for its infection-fighting and cough suppressive qualities. Thyme tea is an old time favorite cough and cold remedy. The essential oils of thyme are grouped into three main types: thyme oil, which contains 42–60% phenols and is mainly thymol; origanum oil, which contains 63–74% phenols and is mainly carvacrol; and lemon thyme oil, which contains citral. The dietary addition of thyme essential oils to the diet at 3 concentrations (5000, 2500 and 1250 ppm) and fed to Balb/c mice. The extent of ear swelling in DTH/CHS reaction, paw edema induced by carrageenan administration and TNBS-induced colitis were evaluated. Dietary supplementation with 5000 ppm of oil decreased paw edema and ear swelling and the microscopic and macroscopic scores of colitis (49).

***Zanthoxylum piperitum*** AP DC (Rutaceae): The major constituents of the essential oil were limonene and geranyl acetate. The oil decreased approximately 38% of nitrite production, as compared to LPS-induced nitrite production. However, the essential oil and its components did not suppress NO chemically in a cell-free system and inhibited iNOS mRNA transcription. The inhibition of E-selectin gene transcription by the oil caused the suppression of cellular adhesion. These

results suggest that the essential oil of this plant might have anti-immunological anti-inflammatory activity (50).

***Zanthoxylum schnifolium*** Sieb. et Zucc.(Rutaceae): This plant has been used in traditional medicine for treatment of the common cold, stomachache and diarrhea (51, 52). The chemical composition of the essential oil was found by GC/MS and 55 compounds were detected. The main constituents were β-phellandrene (22.54%), citronellal (16.48%), and geranyl acetate (11.39%). The oil and its constituents (β-phellandrene, citronellal and geranyl acetate) significantly suppressed gene transcription of iNOS, the COX-2 gene, and biosynthesis of IL-1β by LPS-stimulated macrophage cells. This result suggests that the essential oil may be useful to relief and retardation of immunological inflammatory responses (53).

***Zingiber officinale*** Roscoe (Zingiberaceae): This plant is commonly known as "ginger." It is used in folk medicine to treat pain, inflammation, arthritis, urinary infections, and gastrointestinal disorders. The ginger essential oil at doses of 50, 100 and 200 mg/kg, p.o. significantly suppressed the acetic acid-induced writhing response in a dose-dependent manner. Maximum inhibition of the oil was observed at 200 mg/kg. GEO was found to contain monoterpenes and sesquiterpenes as principal compounds, suggesting that the anti-inflammatory and analgesic effects could be correlated to these essential oil constituents (54).

***Zingiber zerumbet*** (L) Sm. (Zingiberaceae): It is locally known as lempoyang or wild ginger. In traditional medicine is used to cure swelling and loss of appetite. The juice of the boiled rhizomes has also been used as a medicine for worm and ascaris in children (55). The rhizomes' essential oil was evaluated in acute and chronic inflammatory models, using carrageenan-induced paw edema and cotton pellet-induced granuloma, respectively; non-inflammatory-mediated pain was also assessed using a formalin test. The oil exhibited significant anti-inflammatory activity both in acute and chronic inflammation, and also had anti-nociceptive activity (56).

***Zizyphus jujube*** Miller (Rhamanaceae): In traditional medicine it is used in the treatment of diabetes and anti-fertility (57, 58), diarrhea and insomnia. The anti-inflammatory activity of the essential oil obtained from the seeds of *Z .jujube* was evaluated on ear edema induced with TPA in mice. The treatment with 1% and 10% of the essential oil caused significant decreased in ear thicknesses. Furthermore, histological analysis confirmed that this oil inhibited the inflammatory responses of skin inflammation in mice (59).

## Discussion

Inflammatory diseases are generally treated with steroidal and non-steroidal anti-inflammatory drugs (60). However, both of them have significant negative side effects, reducing their use in certain segments of the population (61). Hence, there is a need to develop new drugs with novel modes of action and fewer side effects. The use of herbal therapy or alternative medicine constituents is an attractive approach for the treatment of several inflammatory disorders (62). Essential oils are plant secondary metabolites that are used extensively in aromatherapy and various traditional medicinal systems and many of these oils possesses different pharmacological properties, one of which is the anti-inflammatory effects on several different models of inflammation as shown in this review. A large number of the essential oils contain various bioactive compounds, some of which have potent anti-inflammatory effect including carvacrol, limonene, citronellal, and cinnamaldehyde, among others.

The results presented in this report suggest the applications of essential oils or their components as anti-inflammatory agents and might accelerate the development of new drugs for different inflammatory diseases.

### References


1. C.A. Donanello, Proinflammatory and anti-inflammatory cytokines as mediators in the pathogenesis of septic shock. *Chest*, **112**, 321–329 (1997).
2. M.A.Palladino, F.R. Bahjat, E.A. Theodorakis, L.L. Moldawe, Anti-TNF-alpha therapies: the next generation. *Natl. Rev. Drug Discov.*, **2**, 736–746 (2003).
3. J. Hippisley-Cox and C. Coupland, Risk of myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional *non-steroidal* anti-inflammatory drugs: population based nested case-control analysis. *Br. Med. J.*, **330**, 1366-1369 (2005).
4. M.R. Perrone, M.C. Artesani, C. Viola, F. Gaeta, M. Caringi, D. Quarantino, A. Romano, Tolerability of Rofecoxib in patients with adverse reactions to nonsteroidal anti-inflammatory drugs: A study of 216 patients and literature review. *Int. Arch. Allergy Inmunol.*, **132**, 82-86 ( 2003).
5. R.G. Ogirala, T.K. Aldrich, D.J. Prezant, M.J. Sinnett, J.B. Enden, M.H. Williams, High-dose intramuscular triamcinolone in severe, chronic, life-threatening asthma. *N. Eng. J. Med.*, **324**(9), 585-589 (1991).
6. V. Ballabeni, M.Tognolini, M. Chiavarini, M. Impicciatore, R. Bruni, A. Bianchi, E. Barocelli, Novel antiplatelet and antithrombotic activities of essential oil from *Lavandula hybrida* Reverchon "Grosso". *Phytomed.*, **11**, 596–601 (2004).
7. D.P.M. Jazet, F. Boyom, M.L. Sameza, D.B. Ndongson, N.L. Kwazou, A.P.H. Zollo, C. Menut , Investigations on the essential oils of some *Aframomum* species (Zingiberaceae) from Cameroon as potential antioxidant and anti-inflammatory agents. *Int. J. Esset. Oil Ther.*, **2**, 149-155 (2008).
8. D.P. M.Jazet, F. Tchoumbougnang, S. E. Tchinda, S. Manedong, K., A. P.H. Zollo, C. Menut, Antioxidant and anti-inflammatory potential of essential oils of some *Zanthoxylum* (Rutaceae) of Cameroon. *Int. J. Esset. Oil Ther.*, **2**(2), 82-88 (2008).
9. D.P.M. Jazet, P.M.B. Fekam, M.L. Sameza, D.B. Ndongson, N.L. Kwazou, Investigations of the essential oils of some *Afromomum* species (Zingiberaceae) from Cameroon as potential antioxidant and anti-inflammatory agents. *Int. J. Esset. Oil Ther.*, **2**(4),149-155 (2008).
10. G. Del-Vechio-Vieira, S.O. Vieira, M.M. Abreu, L. Senna-Valle, K.M.A. Coelho, Analgesic and anti-inflammatory properties of essential oil from *Ageratum fastigiatum. Braz. Arch. Biol. Technol.,* **52**(5), 1115-1121 (2009).
11. D.P.M. Jazet, F. Tchoumbougnang, B. Ndongson, W. Aganade, B. Sandjon, A.P.H. Zollo, C. Menut, Chemical characterization, antiradical, antioxidant and anti-inflammatory potencial of the essential oil of *Canarium schweinfurthii* and *Aucoumea klaineana* (Burseraceae) growing in Cameroon. *Agric. Biol. J. North Am.*, **1**(4), 606-611 (2010).
12. M. Apel, M.E.L Lima, M. Sobral, M.C.C. Young, I. Cordeiro, E.E.S. Schapoval, A.T. Henriques, P.R.H. Moreno, Anti-inflammatory activity of essential oil from leaves of *Myciaria tenella* and *Calycorectes sellowianus. Pharm.Biol.*, **48**(4), 433-438 (2010).
13. C.T. Lin, C.J. Chen, T.Y. Lin, J.C. Tung, S.Y. Wang, Anti-inflammation activity of fruit essential oil from *Cinnamomum insularimontanum* Hayata. *Bioresource. Technol.,* **99**(18), 8783-8787 (2008).
14. Y.T. Tung, M.T. Chua, S.Y. Wang, S.T. Chang, Anti-inflammation activities of essential oil and its constituents from indigenous cinnamon (*Cinnamomum osmophloeum*) twigs. *Bioresource Technol.,* **99**, 3908-3913 (2008).

15. P.H. Graham, L. Browne, H. Cox, J. Graham, Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial. *J. Clin. Oncol*., **21**(12), 2372-2376 (2003).
16. M. Karaca, H. Özbek, A. Him, M. Tütüncü, H.A. Akkan, V. Kaplanoglu, Investigation of anti-inflammatory activity of bergamot oil. *Eur. J. Gen Med*., **4**(4), 176-179 (2007).
17. D.P.M. Jazet, J. Kuate, V. Ngouana, F. Damesse, S.E. Tchida, A.P.H. Zollo, C. Menut, Comparison des propiétes antiradicalaines et anti-inflammatoires des huiles essentielles de *Citrus reticulate* var. Madagascar et *Citrus sinensis* var Casagrande du Cameron. *Fruits,* **63**(4), 201-208 (2008).
18. E.J. Yang, S.S. Kim, J.Y. Moon, T.H. Oh, J.S. Baik, N.H. Lee, C.G. Hyun, Inhibitory effects of *Fortunella japonica* var. margarita and *Citrus sunki* essential oils on nitric oxide production and skin pathogens. *Acta Microbiol. Inmunol. Hung.*, **57**(1), 15-27 (2010).
19. N. Thi Dung, V.K. Bajpai, J. In Yoon, S. Chul Kang, Anti-inflammatory effects of essential oil isolated from the buds of *Cleistocalyx operculatus* (Roxb.) Merr and Perry. *Food Chem. Toxicol,* **47**, 449-453 (2009).
20. S.L. Naboruu, C.A. Hiruma and L.C. Di Stassi, Evaluation of antiulcerogenic and analgesic activities of *Cordia verbenaceae* (Boraginaceae). *J. Ethnopharmacol.*, **119**(1), 94-98 (2008).
21. R. Medeiros, G.F. Passos, C.E. Vitor, J. Koepp, T.L. Mazzuco, L.F. Pianowski, M.M. Campos, J.B. Calixto, Effect of two active compounds obtained from the essential oil of *Cordia verbenacea* on the acute inflammatory responses elicited by LPS in the rat paw. *Br. J. Pharmacol.*, **151**, 618-627 (2007).
22. S. Biradar, V.A. Kangralkar, Y. Mandavkar, M. Thakur, N. Chougule. Anti-inflammatory, anti-arthritic, analgesic, and anticolvulsant activity of Cyperius essential oils. *Inter. J. Pharm. Pharm. Sci.* **2**(4), 112-115 (2010).
23. H. Sarma, A. Sarma and C.M. Sarma, Traditional knowledge of weeds: a study of herbal medicines and vegetables used by the Assamese people (India). *Kerba Polnica,* **54**, 80–88 (2008).
24. L.A. Usman, A.A. Hamid, N.O. Muhammad, T.I. Edewore, B.K. Saliu, Chemical constituents and anti-inflammatory activity of leaf essential oil of Nigerian grown *Chenopodium album* L. *EXCLI J*., **9**, 181-186 (2010).
25. I.A. Oyemitan, E.O. Iwalewa, M.A. Akanmu, S.O. Asa, T.A. Olugbade, The Abusive Potential of Habitual Consumption of the Fruits of *Dennettia tripetala* G. Baker (Annonaceae) Among the People in Ondo Township (Nigeria). *Nig. J. Natural Products Med.,* **10**, 55-62 (2006).
26. I.A. Oyemitan, E.O. Iwalewa, M.A. Akanmo, T.A. Olugbade, Antinociceptive and anti-inflammatory effects of essential oil of *Dennettia tripetala* G. Baker (Annonaceae) in rodents. *Afr. J. Trad. CAM.* **5**(4), 355-362 (2008).
27. L.H.J. Lago, L.A.C. Carvalho, F.S. Silva, D.O. Toyama, O.A. Fávero, P. Romoff, Chemical composition and anti-inflammatory evaluation of essential oils from leaves and steam barks from *Drimys brasiliensis* (Winteraceae). *J. Braz. Chem. Soc.,* **21**(9), 1760-1765 (2010).
28. Y. Lu, C.X. Zhong, L. Wang, C. Lu, X.L. Li., P.J. Wang, Anti-inflammation activity and chemical composition of flower essential oil from *Hedychium coronarium. Afri. J. of Biotechnol*. **8**(20), 5373-5377 (2009).
29. J.Y. Kim, S.S. Kim, T.H. Oh, J.S. Baik, G. Song, N.H. Lee, C.G. Hyun, Chemical composition, antioxidant, anti-elastase, and anti-inflammatory activities of *Illicium anisatum* (Illiciaceae) essential oil. *Acta Pharm*. **59**, 289-300 (2009).
30. M.M.V. Barros, L.A.K. Rocha de Melo, B.L. Medeiros, S. Maia de Morais, N.D.C. Sousa, Topical anti-inflammatory, gastropotective and antioxidant effects of the essential oil of *Lippia sidoides* Cham. Leaves. *J. Ethnopharmacol*, **111**, 378-382 (2007).
31. R. Vila and S. Cañigueral, Aceite esencial de *Malaleuca alternifolia* en el tratamiento de vulvovaginitis. *Fitoterapia.,* **6**(2), 119-128 (2006).
32. O.D. Moronkola, I.A. Oladosu, A. Adeleke, M.S. Ali, Chemical composition and anti-inflammatory activity of the essential oil of the aerial part of *Mezoneuron benthamianum* Baill. (Caesalpinoideae). *European J. Appl. Sci*. **1**(3): 30-33 (2009).
33. M. Apel, M.E.L. Lima, M. Sobral, M.C.C. Young, I. Cordeiro, E.E.S. Schapoval, A.T. Henriques, P.R.H. Moreno, Anti-inflammatory activity of essential oil from leaves of *Myciaria tenella* and *Calycorectes sellowianus*. *Pharm. Biol*., **48**(4), 433-438 (2010).
34. L.C. Smitherman, J. Janisse and A. Mathur, The use of folk remedies among children in an urban black community: remedies for fever, colic, and teething. *Pediatrics*, **115**(3), 297-304 (2005).
35. R.E Lopes, T.D. Oliveira, L.J.H. Guilardi, P. Romoff, K.T. Berti, M.T. Reis-Silva, M.M. Bernardi, Anti-nociceptive and anti-inflammatory actions of *Nepeta cataria* L. var. citriodora (Becker) Balb. essential oil in mice. *J. Health Sci. Inst.* **28**(3), 289-293 (2010).
36. R. Bruni, A. Medici, E. Andreotti, C. Fantin, M. Muzzoli, M. Dehesa, C. Romagnoli, G. Sacchetti, Chemical composition and biological activities of Ishpingo essential oil, a traditional Ecuatorian spice from *Ocotea quixos* (Lam.) Kosterm. (Lauraceae) flower calices. *Food Chem*. **85**, 415–21 (2004).
37. V. Ballabeni, M. Tognolini, C. Giorgio, S. Bertoni, R. Bruni, E. Barocelli, *Ocotea quixos* Lam. Essential oil: *In vitro* and *in vivo* investigation on its anti-inflammatory properties. *Fitoterapia,* **81**(4), 289-295 (2009).
38. E. Haloui, Z. Marzouk, B. Marzouk, I. Bouftira, A. Bouraoui, N. Fenina, Pharmacological activities and chemical composition of *Olea europea* L. leaf essential oil from Tunisia. *J. Food Agri. Env.,* **8**(2), 204-208 (2010).
39. M.R. Loizzo, F. Menichini, F. Confort, R. Tundis, M. Bonesi, A.M. Saab, G.A. Statti, B. Cindio, P.J. Houghton, F. Menichini, N.G. Frega, Chemical analysis, antioxidant, anti-inflammatory and anticholinesterase activities of *Origanum ehrenbergii* Boiss and *O. syriacum* L. essential oils. *Food Chem.*, **117**, 174-180 (2009).
40. A. Ocana-Fuentes, E. Arranz-Gutierrez, E. Senorans, Supercritical fluid extraction of oregano (*Origanum vulgare*) essential oils: Anti-inflammatory properties based on cytokine response on THP-1 macrophages. *Food Chem. Toxicol.* **48**, 1568-1575 (2010).
41. M. Lis-Balchin, Ed., *Geranium pelargonium*, Taylor & Francis, London and New York (2002)
42. A. Elmann, S. Mordechay, M. Rindner, U. Ravid, Anti-neuroinflammatory effects of geranium oil in microglial cells. *J. Functional Foods*, **2**(1), 17-22 (2010).
43. T.N. Tabanka, E. Bedir, N. Kirimer, K.H. Basser, S.I. Khan, M.R. Jacob, I.A. Khan, Antimicrobial compounds from *Pimpinella* species growing in Turkey. *Planta Med.,* **69**, 933–938 ( 2003).
44. N. Tabanca, G. Ma, D.S. Pasco, E. Bedir, N. Kirimer, S.I. Khan, K.H. Basser, Effect of essential oil and isolated compounds from *Pimpinella* species on NF-κB: A target for anti-inflammatory therapy. *Phytother. Res.,* **21**, 741-745 (2007).
45. S. Darshan and R. Doreswamy, Patented antiinflammatory plant drug development from traditional medicine. *Phytother Res.,* **18**, 343-357 (2004).
46. S .Juha, A. Bukovska, S. Cikos, S. Czikkva, D. Fabian, J. Koppel, Anti-inflammatory effects of *Rosmarinus officinalis* essential oil in mice. *Acta Vet. Brno,* **78**(1), 121-127 (2009).
47. C. Erichsen-Braun; *Medicinal and Other Uses of North America Plant.* Dover Publications, 1989.
48. A.A. Sherifat, A.I. Oladosu and A.O. Isiaka, Topical anti-inflammatory activity and chemical composition of essential oil of *Sabina virginiana* L. Antoine (Cupressaceae). *Arch. Appl. Sci. Res.,* **2**(2), 1-6 (2010).
49. S. Juhás, D. Bunakova, P. Rehak, S. Cikos, S. Czikková, J. Veselá, G. Ilková, J. Koppel, Anti-inflammatory effects of thyme essential oil in mice. *Acta Vet. Brno.,* **77**, 327-334 (2008).
50. J.H. Lee, K.M. Chang and G.H. Kim, Anti-inflammatory activities of Chopi (*Zanthoxylum piperitum* AP DC) essential oil: suppression of the inducible nitric oxide synthase and cellular adhesion. *Food Sci. Biotechnol*., **18**, 123-132 (2009).
51. Y.J. Choi, *The Korean Folklore Plants.* Academybook, Seoul (1992).
52. Y.S. Ko and H.J. Han, Chemical constituents of Korean chopi (*Zanthoxylum piperitum*) and sancho *(Zanthoxylum schnifolium). Korean J. Food Sci Technol.,* **28**, 19–27 (1996).
53. J.H. Lee, K.M. Chang and G.H. Kim, Composition and anti-inflammatory activities of *Zanthoxylum schinifolium* essential oil: suppression of inducible nitric oxide synthasa, cyclooxygenase-2, cytokines and cellular adhesion. *J. Sci. Food Agri.,* **10**, 1762-1769 (2009).
54. A. Vendruscolo, I. Takaki, L.E. Bersani-Amado, J.A. Dantas, C.A. Bersani-Amado, R.K.N. Cuman. Anti-inflammatory and antinociceptive activities of *Zingiber officinale* Roscoe essential oil in experimental animal models. *Indian J. Pharmacol*. **38**(1), 58-59 (2006).
55. R. Omar, Z. Ali Rahman, M.T. Latif, T. Lihan, J.H. Adam. (Eds.) Proceedings of the Regional Symposium on Environment and Natural Resources Malaysia. **1**, 516-520 (2002).

56. Z.A. Zakaria, A.S. Mohamad, M.S. Ahmad, A.F. Mokhtar, D.A. Israf, N.H. Lajis, M.R. Sulaiman, Preliminary analysis of the the anti-inflammatory activity of essential oils of *Zingiber zerumbet. Published online Nov 26, doi: 10:1177/1099800410386590 (2010).*
57. S.P. Ambasta, *Useful Plants of India*. pp.703 Publications and Information Directorate, CSIR, New Delhi, India (1986).
58. A. Erenmemisoglu, F. Keletimur, A.H. Koker, H. Utsuol, Y. Tekol, M.Ustdal, Hypoglycemic activity of *Zizyphus jujuba. J. Pharm. Pharmacol.*, **47**, 72–74 (1995).
59. S.M. Al-Reza, J.I. Yoon, H.J. Kim, J.S. Kim, S.C. Kang, Anti-inflammatory activity of seed essential oil from *Zizyphus jujube. Food Chem. Toxicol.*, **48**, 639-643 (2010).
60. M.J.S. Langman, Ulcer complications and non-steroidal anti-inflammatory drugs. *Am. J. Med. (Suppl.),* **84**(2), 15-19 (1988).
61. P. Juni, S. Reichenbach and M. Egger, COX2 inhibitors, traditional NSAIDs and the heart. *Br. Med. J.,* **330**, 1342-1343 (2005).
62. J.B. Calixto, M.M. Campos, M.F. Otuki, A.R. Santos, Anti-inflammatory compounds of plant origin. Part II. Modulation of pro-inflammatory cytokines, chemokines and adhesion molecules. *Planta Med.,* **70**, 93–103 (2004).